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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,976	04/28/2006	Thomas Rueckle	283829US0PCT	9518

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER

HAVLIN, ROBERT H

ART UNIT	PAPER NUMBER
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1626

NOTIFICATION DATE	DELIVERY MODE
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03/08/2011

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/565,976	Applicant(s) RUECKLE ET AL.	
	Examiner ROBERT HAVLIN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 February 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 3,6,9,10,12-20 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,11 and 21 is/are rejected.
- 7) ☒ Claim(s) 7 and 8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/19/11</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

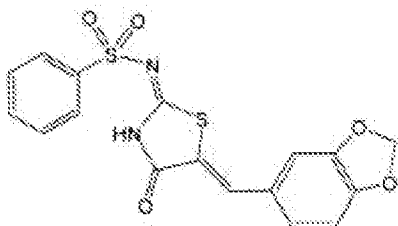
Status of the claims: Claims 1-22 are currently pending.

Priority: This application is a 371 of PCT/EP04/51625 (07/27/2004) and claims priority to EUROPEAN PATENT OFFICE (EPO) 03102313.8 (07/28/2003).

IDS: The IDS dated 1/19/2011 was considered.

Election/Restrictions

1. Applicant previously elected Group I (claims 1-11 and 21) and the following species (allegedly reading on claims 1, 2, 4, 5, 7, 8, 11, and 21):



As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and claims not reading on the elected species are held withdrawn. Accordingly, claims 3, 6, 9, and 10 are hereby withdrawn.

Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP 803.02.

RESPONSE TO APPLICANT REMARKS

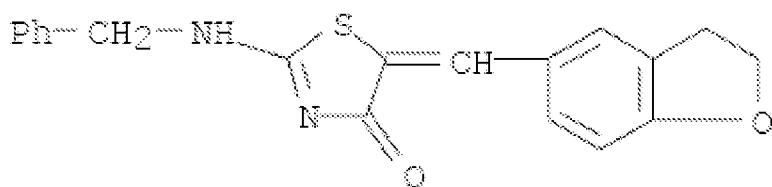
Claim Rejections - 35 USC § 112

2. Claims 1, 2, 4, 5, 11, and 21 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant has amended the claims to more clearly define the scope of "G." Therefore, this rejection is **withdrawn**.

Claim Rejections - 35 USC § 102

3. Claims 1, 4, 11, and 21 were rejected under 35 U.S.C. 102(e) as being anticipated by Hasegawa et al. (US 2006/0293338).

Hasegawa teaches the following compound as a pharmaceutical agent:



Applicant deleted the alternative "alkyl aryl" from the definition of G, therefore the rejection is **withdrawn**.

NEW CLAIM REJECTIONS

Claim Rejections - 35 USC § 112

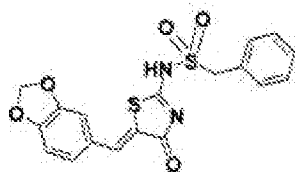
4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 4, 5, 11, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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The claims provide a "proviso" for compounds that do not appear to be within the claim scope when given the broadest reasonable interpretation. For example, the following proviso-ed compound:



is no longer part of the claim scope due to the amendment of "G."

As a result, one of ordinary skill in the art would be confused as to what applicant intends to claim and is ambiguous with respect to whether "alkyl-aryl" remains within the claim scope. Thus, the claim is rejected.

The examiner recommends deleting proviso-ed alternatives that would result in confusion regarding the metes and bounds of the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

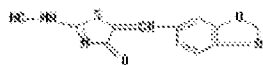
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. Claims 1, 2, 4, 5, 11, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoneda et al. (US 5750712) in view of Unangst et al. (J. Med. Chem., 1994, Vol. 37, No. 2, p. 322-28).

1. Determining the scope and contents of the prior art.

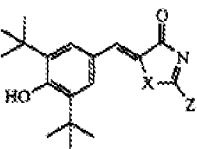
Yoneda et al. (US 5750712) teaches pharmaceutical compounds closely structurally related to the instant claims including the following species:



In col. 2, Yoneda describes the success of Unangst et al. using related compounds for achieving cyclooxygenase inhibiting activity.

Unangst et al. (J. Med. Chem., 1994, Vol. 37, No. 2, p. 322-28) teaches inter alia:

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Table 3. Biochemical and in Vivo Antiinflammatory Activity of Benzylidene Derivatives 6-9


no.	X	Z	IC ₅₀ , μM ^a		CFE ^b inhib ± SEM at dose in mg/kg po		MFE ^c ID ₅₀ , mg/kg po
			5-LO	CO	30	10	
6a	S	OH	1.4	0.35	59 ± 4.6 ^d	54 ± 4.3	2.0 (1.0-3.2) ^d
6c	S	SH	0.38	0.012	36 ± 5.0 ^e	32 ± 4.4	
6f	S	NH ₂ -MeSO ₃ H	0.77	0.39	61 ± 4.5	52 ± 3.6	0.6 (0.3-0.9)
6g	O	SH	0.84	1.7	40 ± 2.9	32 ± 6.5	12.4 (8.0-20.2)
6i	NMe	OH	0.78	4.6	N ^f		
6j	NMe	SH	0.17	0.79	N		
6k	CH ₃	SH	1.7	2.4	39 ± 3.9	19 ± 4.7	N ^g
7a	S	SMe	0.66	0.80	47 ± 7.1	36 ± 6.2	N
8a	S	NHMe	N ^h	N			
8b	S	NMe ₂	65 ⁱ	N			
8c	S	NHOH	3.7	0.80	N ^j		
8e	S	NMeOH	7.3	10.0	N		
8f	S	NHOMe	N	61 ⁱ			
8h	S	NMeOMe-HCl	1.7	0.33	36 ± 2.7	41 ± 3.6	6.2 (2.4-11.8)
8i	S	NHCN	0.63	0.16	49 ± 5.9 ^k	29 ± 4.4	N ^k
8l	S	NHCNHNH ₂ -HCl	0.91	0.083	40 ± 3.1	34 ± 5.4	2.2 (0.8-3.9)
8m	S	NHCNHNMe ₂	100 ^l	N			
8n	S	NH(CH ₂) ₂ NMe ₂	79 ⁱ	N			
8o	S	NH(CH ₂) ₃ CO ₂ H	53 ⁱ	N			
8q	O	NHCN-choline	2.6	1.1	N		
8s	O	NHCNHNH ₂ -MeSO ₃ H	1.2	0.34	48 ± 3.3	33 ± 4.0	5.7 (4.1-7.5)
8t	NMe	NHCN	0.70	3.5	N ^l		
8v	NMe	NHCNHNH ₂	1.3	2.1	N		
9b	O	OH-choline	2.8	0.65	51 ± 2.7	35 ± 3.6	3.7 (2.4-5.0)
1a			2.5	0.15	28 ± 5.1	17 ± 9.5	3.7 (2.0-7.2)
1b			0.56	0.040	26 ± 4.7	29 ± 3.1	1.9 (1.1-2.9)
sodium meclofenamate			24.0	0.10	41 ± 5.3	34 ± 5.5	0.40 (0.02-1.0)

Specifically, the reference teaches the compound "8f" as having activity.

2. Ascertaining the differences between the prior art and the claims at issue.

The difference between the prior art and the claims is a cyano vs. methoxy substitution at the "G" position as described in the instant claims.

3. Resolving the level of ordinary skill in the pertinent art.

One of ordinary skill in the art would consider it routine to modify the chemical structure of a pharmaceutical compound in an effort to produce a new compound with improved properties.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The record does not contain evidence of any secondary considerations.

One of ordinary skill in the art would be motivated to combine the Yoneda and Unangst due to both the specific reference of Unangst in Yoneda as well as the structural similarity of the compounds taught by each. One of skill in the art would recognize the potential for modifying the “G” group due to Unangst teaching in Table 3. Based on the experimental data establishing the activity of the –NHOMe group of compound 8f (wherein the “G” group as per the instant claims is –OMe), one of skill in the art would be suggested to modify the G group of Yoneda to a –OMe. In addition, based on the structural similarities of the two prior art references, one of ordinary skill in the art would also have a reasonable expectation that the modification would result in similar activity.

In *Eisai Co. Ltd. v. Dr. Reddy's Laboratories Ltd.*, 87 USPQ2d 1452, 1454 (Fed. Cir. 2008), the Federal Circuit clarified the proof of obviousness in structural similarity situations such as this:

Where, as here, the patent at issue claims a chemical compound, the analysis of the third Graham factor (the differences between the claimed invention and the prior art) often turns on the structural similarities and differences between the claimed compound and the prior art compounds. See *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1377 [81 USPQ2d 1324] (Fed. Cir. 2006) (noting that, for a chemical compound, a prima facie case of obviousness requires “structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions” (quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc))). Obviousness based on structural similarity thus can be proved by identification of

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some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound. See *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 [83 USPQ2d 1169] (Fed. Cir. 2007). In keeping with the flexible nature of the obviousness inquiry, *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 [82 USPQ2d 1385] (2007), the requisite motivation can come from any number of sources and need not necessarily be explicit in the art. See *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1301 [84 USPQ2d 1198] (Fed. Cir. 2007). Rather “it is sufficient to show that the claimed and prior art compounds possess a ‘sufficiently close relationship ... to create an expectation,’ in light of the totality of the prior art, that the new compound will have ‘similar properties’ to the old.” *Id.* (quoting *Dillon*, 919 F.2d at 692).

In the instant case, the prior art does possess a close structural relationship when the elected species is compared to the compound of Yoneda and the motivation to combine and modify is provided therein and by Unangst, thus a prima facie case of obviousness is established.

Claim Objections

Claims 7, and 8 are objected to for being dependent on a rejected base claim and reading on subject matter beyond the restricted scope.

Conclusion

The claims are not in condition for allowance. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Primary Examiner, Art Unit 1626